Arg	Lys 290	Val	Leu	Glu	Leu	Ala 295	Ala	Ala	Leu	Ser	Asp 300	Asp	Phe	Glu	Arg	
Ala 305		Arg	Arg													
(2)	IMPO	Jema:	eion	FOR	880	m i	<b>8</b> 0: 3	95÷								
	(3.)		(A) (B) (C)	CE CI LENG' TYPE: STRAI TOPOI	TH: : : now : deci	)4 ba :lei: :ESS:	ase : C ac: : si:	pair: id	5							
	( <b>xi</b> )	) SE	Öüza	CE DI	escr:	eptic	ON: S	SEQ :	ID XX	); 95	5 ¢					
AAGI	acttac	Bat :	CHAR	G <b>at</b> o:	ac ce	iaggi	atst	r ca	Ca							34
(2)	Inp	orma'	TION	FOR	SEQ	id i	MO: 1	96:								
	(£)		(A) (B) (C)	CE CI LENCI TYPE STRAI TOPOI	TH: 1 DUM SDEDI	l7 bi zlei: WESS	ase ; c &c: : si:	pair: (d	§:							
	(xx)	) se	QUEN	CE DI	escr:	Pri	ON: S	SEQ :	ID W	); 9(	S x					
C984	COAC	aac (	ggat	CCTA	CC GK	GTC	36									27
(2)	INT	ORMA	TICN	FOR	SRQ	id i	MO: S	97:								
	(i)		(A) (S) (C)	CE CI LSNG TYPE STRAI TOPO)	rn: : nu: Wedi	20 b: Clei: WESS	ase j c ac: : si:	pair id	\$							
	(xi	) 58	ÇÜEN	CB D	escr:	ipti:	OM: :	SEQ :	ID M	); 9°	) z					
				TGGA												28
(2)	INF			FOR												
	11		(A) (B) (C)	CE C: LENG: TYPE STRA: TOPO:	CH: : : nu: : nu:	25 b: clei: WESS	ase ; c ac: : si:	pair: id	\$							

 -0.4	
 Σ.5	50.
 ~ 3	8.76

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 98:	
GACGAGATCT TATGGGCTTA CYGAC	25
{2} INFORMATION FOR SEQ ID NO: 99:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 33 base pairs  (B) TYPS: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
(xí) SEQUENCE DESCRIPTION: SEQ ID NO: 99:	
CCCCCCAGAT CTGCACCACC GGCATCGGCG GGC	33
(2) INFORMATION FOR SEQ ID NO: 100	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 26 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 100:	
GCBGCGGATC CGTTGCTTAG CCGG	24
(2) INFORMATION FOR SEQ ID NO: 101:	
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 base pairs (S) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 161:	
CCGGCTGAGA TCTATGACAG AATACGAAGG GC	32
(2) INFORMATION FOR SEQ ID NO: 182:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 24 base pairs  (B) TYPE: mucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
(*i) SEQUENCE DESCRIPTION: SEQ ID NO: 102:	
CCCCGCCAGG GAACTAGAGG CGGC	34
(3) INFORMATION FOR SEQ ID NO: 103:	

		207

	(ž)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 38 base pairs  (B) TYPE: nucleic scid  (C) STRANDEUNESS: single  (D) TOFOLOGY: linear	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 103:	
CTGC	CGAGA	T CTACCACCAT TGTCGCGCTG AAATACCC	38
(2)	infor	MATION FOR SEQ ID NO: 104:	
	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 104:	
cacc	atecc	C TYACGEGEEA ACTEG	25
(2)	INFOR	MATION FOR SEQ ID NO: 105:	
	<b>(</b> ±)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 32 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 105:	
aaca	GAGAT	C TOTGAGTTTT CCGTATTTCA TC	32
(2)	INFOR	MATION FOR SEQ ID NO: 106:	
	(1)	SEQUEBCE CHARACTERISTICS:  (A) LEMSTH: 25 base pairs  (B) TYPE: nucleic acid  (C) STWANDEDNESS: single  (D) TOPOLOGY: linear	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO: 106:	
CGCG	TCGAG	C CATSGITAGG CGCAG	28
(2)	INFOR	MATION FOR SEQ ID NO: 107;	
	(i)	SEQUENCE CHARACTERISTICS:  {A} LENGIH: 32 base pairs  {B} TYPE: nucleic acid  {C} STRANDEDNESS: single  {D} TOPOLOGY: linear	

	574	35
- 2	3.3	24

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 107:	
GAGGAAGATC TATGACAACT TCACCCGACC CG	32
{2} INFORMATION FOR SEQ ID NO: 108:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 28 base pairs  (B) TYPE: nucleic scid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 108;	
CATGAAGCCA TGGCCCGCAG GCTGCATG	28
(2) INFORMATION FOR SEQ ID NO: 109:	
(i) SEQUENCE CHAFACTERISTICS: (A) LENGTH: 33 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 109:	
GGCCGAGATC TGTGACCCAC TATGACGTCG TCG	33
(2) INFORMATION FOR SEQ ID NO: 110:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 36 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
(*i) SEQUENCE DESCRIPTION: SEQ ID NO: 110:	
GGCGCCCATG GTCAGAAATT GATCATGTGG CCAACC	36
(2) INFORMATION FOR SEQ ID NO: 111:	
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 33 base pairs (B) TYPR: nucleic scid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 111:	
CCGGGAGATC TATGGCAAAG CYCYCCACCG ACG	33
(2) INFORMATION FOR SEQ ID NO: 112;	

	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 32 base pairs  (B) TYPE: mucleic scid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 112:	
cact	TEGECAG AGCTACTTEA CEGTUACEGT GG	32
(2)	INFORMATION FOR SEQ ID NO: 113:	
	(1) SEQUENCE CHARACTERISTICS: (A) LHWITH: 36 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 113:	
98CC	CASATC TATESCCATT SAGGTTTCES TETTESC	36
(2)	INFORMATION FOR SEQ ID NO: 114:	
	(i) SEQUENCE CHARACTERISTICS: {A} LENGTH: 26 base pairs {B} TYPE: nucleic scid {C} STRANDEDNESS: single {D} TOPOLOGY: linear	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 114:	
cacc	DETETTS CATGGCAGCS CTGAGC	26
(2)	INFORMATION FOR SEQ ID NO: 115:	
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 24 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 115:	
GGAC	COTTCAR GCGACACATC GCCG	24
(2)	INFORMATION FOR SEQ ID NO: 116:	
	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 24 base pairs (B) TYPS: nucleic scid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	

1	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 116:	
CAGCA	ACGAAC GCCCCTTCGA TOGC	24
(2) 3	INFORMATION FOR SEQ ID NO: 117;	
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 16 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
8	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 117:	
acagi	RTCTGT GACEGACATE AACCCG	26
(2) 1	INFORMATION FOR SEQ ID NO: 118:	
	(i) SEQUENCE CHARACTERISTICS: (A) LINGTH: 28 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
4	(*i) SEQUENCE DESCRIPTION: SEQ ID NO: 118:	
ZTTE	CCATGG TCACGGGCCC COGGTACT	28
(2)	INFORMATION FOR SEQ ID NO: 119:	
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 36 base pairs  (B) TYPE: nucleic scid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
;	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 119:	
acagi	ATCTOT GCCCATGGCA CAGATA	26
(2)	INFORMATION FOR SEQ ID NO: 120:	
	(i) SEQUENCE CHARACTERISTICS: (A) LEMSTH: 27 base pairs (B) TYPE: sucleic acid (C) STRANDEDNESS: single (D) TOPOLOSY: linear	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 120:	
TTTA	ABCTTC TAGGCGCCCA GCGCGGC	27
3 % Q Q	TRECORMANTING SOME OUR IN 1870, 707,	

(1) SEQUENCE CHARACTERISTICS:  (A) LEBUTH: 26 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOSY: linear	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 121:	
ACAGATCTOC GCATGCOGAT COGTOT	26
(2) INFORMATION FOR SEQ ID NO: 122:	
(i) SEQUENCE CHABACTERISTICS:  (A) LENGTH: 28 base pairs  (B) TYPE: nucleic acid  (C) STRAMDEDNESS: single  (D) TOPOLOSY: linear	
(*i) SEQUENCE DESCRIPTION: SEQ ID NO: 122:	
TTTTCCATUG TCATCCGGCG TGATCGAG	28
(2) INFORMATION FOR SEQ ID NO: 123;	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 25 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 123:	
ACAGATOTOT AATGGCAGAC TOTGAT	36
(2) INFORMATION FOR SEQ ID NO: 124:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 28 base pairs  (B) TYPE: nucleic acid  (C) STRANDEOMESS: single  (D) TOPOLOGY: lines:	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 124:	
TTTTCCATGG TCAGGAGATG GTGATGGA	28
(2) IMPORMATION FOR SEQ ID NO: 125:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 26 base pairs  (B) TYPE: nucleic acid  (C) STRANDEUNESS: single  (D) TOPOLOGY: linear	

212 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 125: ACAGATOTGO CGGCTACCCC GGTGCC 26 (2) INFORMATION FOR SEQ ID NO: 126: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 28 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (x1) SEQUENCE DESCRIPTION: SEQ ID NO: 126: TTTTCCATGG CTATTGCAGC TTTCCGGC 28 (2) IMPORMATION FOR SEQ ID NO: 127: (i) SEQUENCE CHARACTERISTICS: (A) LEMUTH: 50 amino acids (B) TYPE: amino acid (C) STRANDEONESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: None (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 127: Ala Glu Asp Val Arg Ala Glu Ila Val Ala Ser Val Lau Glu Val Val Val Asn Glu Gly Asp Gln Ile Asp Lys Gly Asp Val Val Val Leu Leu Glu Ser Met Tyr Met Glu Ile Fro Val Leu Ala Glu Ala Ala Gly Thr 43 Val Ser \$0 (2) INFORMATION FOR SEQ ID NO: 128: (i) SEQUENCE CHARACTERISTICS: (A) LEMTTH: 49 amino acids (S) TYPE: amino acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPS: None (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 128: Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val 1 3

Val Asn Glu Gly Asp Gln Ile Asp Lys Gly Asp Val Val Leu Leu

25

213 Glu Ser Met Met Glu Ile Pro Val Leu Ala Glu Ala Ala Gly Thr Val 3.5 40 Ser {2} INFORMATION FOR SEQ ID NO: 129: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 50 amino acids (B) TYPE: amino acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: None (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 129: Ala Glu Asp Val Arg Ala Glu Ile Val Ala Ser Val Leu Glu Val Val Val Asn Glu Gly Asp Gln Ile Asp Lys Gly Asp Val Val Val Leu Leu 35 Glu Ser Met Lys Met Glu Ile Pro Val Leu Ala Glu Ala Ala Gly Thr 48 Val Ser 50 (2) INFORMATION FOR SEQ ID NO: 130: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 33 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 130: COGGGAGATO TATOGCAAAG CTCTCCACCG ACG 33 (2) INFORMATION FOR SEQ ID NO: 131; (1) SEQUENCE CHARACTERISTICS: (A) LEMSTH: 32 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 131:

CGCTGGGCAG AGCTACTTGA CGGTGACGGT GG
(2) INFORMATION FOR SEQ ID NO: 132:

(1) SEQUENCE CHARACTERISTICS: (A) LENGTH: 36 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 132:	
OUCOUCUGEA AUCTIGUCAT GACAGAGCAG CAGTOG	36
(2) INFORMATION FOR SEQ ID NO: 133:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 26 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
(x1) SEQUENCE DESCRIPTION: SEQ ID NO: 133:	
CGAACTCGCC GGATCCCCTG TTTCGC	26
(2) INFORMATION FOR SEQ ID NO: 134:	
(i) SEQUENCE CHARACTERISTICS:  {A} LENGTH: 32 hase pairs  {B} TYPE: nucleic acid  {C} STRANDEDNESS: single  {D} TOPOLOGY: linear	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 134:	
GGCAACCGCG AGATCTTTCT CCCGGGCGGGG GC	32
(2) INFORMATION FOR SEQ ID NO: 135:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 27 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 135;	
GCCAAGCTTG COGGCGCCTA ACGAACT	27
(2) INFORMATION FOR SEQ ID NO: 136:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTE: 30 base pairs  (B) TYPE: nucleic acid  (C) STEANDEDNESS: single  (D) TOPOLOGY: linear	

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(x1) SEQUENCE DESCRIPTION: SEQ ID NO: 136:	
GGACCCAGAT CTATGACAGA GCAGCAGTOG	30
(2) INFORMATION FOR SEQ ID NO: 137:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 47 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 137:	
COSSCASCCC CSSCCSGGAG AAAASCTTYS CSAACATCCC ASTGACS	<b>6</b> 7
(2) INFORMATION FOR SEQ ID NO: 138:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 44 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
(*i) SEQUENCE DESCRIPTION: SEQ ID NO: 138:	
GTTCGCARAG CTTTTCTCCC GGCCGGGGCT GCCGGTCGAG TACC	44
(2) INFORMATION FOR SEQ ID NO: 139:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 20 base pairs  (B) TYPE: nucleic scid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 139:	
CCTTCGGTGG ATCCCGTCAG	20
(2) INFORMATION FOR SEQ ID NO: 140:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 450 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
(ix) FEATURE:	
(A) NAME/KEY: Coding Sequence (B) LOCATION: 68346 (D) OTHER INFORMATION:	

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(xi) SECUENCE DESCRIPTION: SEC ID NO: 140:

	~				4
TGGCGCTGTC	ACCGAGGAAC	CTGTCAATGT	CGTCGAGCAG	TACTGAACCG	TTCCGAGAAA

GGCCLAGO ATG AAC GTC ACC GTA TOO ATT COG ACC ATC CTG CGG CCC CAC 109
Met Asn Val Thr Val Ser Ile Pro Thr Ile Leu Arg Pro His
1 5 10

80

ACC GGC GGC CAG AAG AGT GTC TCG GCC AGC GGC GAT ACC TTG GGT GCC 157
Thr Gly Gly Gln Lys Ser Val Ser Ala Ser Gly Asp Thr Leu Gly Ala
15 20 25 30

GTC ATC AGC GAC CTG GAG GCC AAC TAT TCG GGC ATT TCC GAG CGC CTG 205
Val lie Ser Asp Leu Glu Ala Asm Tyr Ser Gly lie Ser Glu Arg Leu
35 40 85

ATG GAC CCG TCT TCC CCA GGT AAG TTG CAC CGC TTC GTG AAC ATC TAC 253
Met Asp Pro Ser Ser Pro Gly Lys Leu His Arg Phe Val Asn Ile Tyr
50 55 60

OTC AAC GAC GAG GAC GTG CGG TTC TCC GGC GGC TTG GCC ACC GCG ATC

Val Asn Asp Glu Asp Val Arg Phe Ser Gly Gly Leu Ala Thr Ala Ile

65 70 75

GCT GAC GGT GAC TCG GTC ACC ATC CTC CCC GCC GTG GCC GGT GGG TGAGC 351 Ala Asp Gly Asp Ser Val Thr Ile Leu Pro Ala Val Ala Gly Gly 80 85 90

GGAGCACATG ACACGATACG ACTCGCTGTT GCAGGCCTTG GGCAACACGC CGCTGGTTGG 411
CCTGCAGCGA TTGTCGCCAC GCTGGGATGA CGGGCGAGA 450

## (2) INFORMATION FOR SEC ID NO: 141:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 93 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- (v) FRAGMENT TYPE: internal
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 141:

Mot Asm Val Thr Val Ser Ile Pro Thr Ile Leu Arg Pro His Thr Gly
1 5 10 15

Gly Gln Lys Ser Val Ser Ala Ser Gly Asp Thr Leu Gly Ala Vel Ile 20 25 38

Ser Asp Leu Glu Ala Asn Tyr Ser Gly Ila Ser Glu Arg Leu Mat Asp 35 40 45

Pro Ser Ser Pro Gly Lys Leu Hiz Arg Phe Val Azn Ele Tyr Val Azn 50 55

Asp 85	Slu	Asp	Val	Arg	Phe 70	Ser	Gly	Gly	Leu	Ala 75	Thr	Ala	Ile	aza	qaA 08	
Gly	Asp	Ser	Va1	Thr	ïle	Leu	Pro	Ala	Val 90	Als	Gly	Gly				
(2)	INFC	SEC	XJEN.	e c	iarac	TER)	cstic	 								
		4	(B) 7 (C) 9	.enco Type : Trai Topoi	nus IDEDI	ilei: MESS:	s aci	Ed	rs							
	(ix)	fri	VTURE	Š:												
		į	(B) I	iame / Jocat Ithei	TON:	88	31	31	ænc	\$						
	(xi)	SEÇ	)(JENC	e di	(SCR)	PTI(	M; S	ssq :	id in	): 14	\$2:					
ggw	ITTC	cos (	ceecc	ceec	a w	IACA	ACAG:	r ca	ngr	CAT	GAC	aacii:	CAC /	aggri	attagg	60
rou	aggti	rca j	CAA	igagi	IC AC	ROCA									NT COS Sp Pro	114
	GCG Ala															162
	GAG Glu															210
	gcg Ala															258
	CAG Gln															306
	CST Arg 75															354
	Ala								Tab	cerc	agc	cacr	GCAG	CA C	AMIACT	408
dedata	acaa	3CG )	raggi	ncar	ia G	gtto	gate	a cc	rtca.	acta	TCA	GTTC	ggt (	gatg:	rogaos	468
CTC	atgg:	cac :	CA									,				480

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(2)	INFO	RMAI	rion	FOR	880	ID :	<b>80</b> 0 3	(43:									
	(\$)	:	(D) 1	ero: Pype : Fyra:	CH: : : ami WED:	:9 ar ino s MESS :	sino scid : si:	acio	is								
			Jecui Vgmei					<u>.</u>									
	( <b>%</b> i)	SBÇ	)uesk	e di	escri	(PTIC	) (1	980	ed w	): 1:	13:						
Met 1	Ala	Thr	Arg	Phe S	Met	Thr	Asp	Pro	His 18	Als	Met	Arg	Asp	Met 15	Ala		
@1y	Arg	Phe	Glu 20	Val	His	Ala	Sin	Thr 25	Val	Glu	Asp	Glu	Ala 30	Arg	Arg		
Met	Trp Ala Ser Ala Gln Asn Ile Ser Gly Ala Gly Trp Ser Gly Met 35 40 45  Glu Ala Thr Ser Leu Asp Thr Met Ala Gln Met Asn Gln Ala Phe 50 55 60																
Ala	. Glu Ala Thr Ser Leu Asp Thr Met Als Gln Met Asn Gln Ala Phe 50 55 60 ; Asn Ile Val Asn Met Leu His Gly Val Arg Asp Gly Leu Val Arg																
Arg 65	Glu Ala Thr Ser Leu Asp Thr Met Ala Glo Met Aso Glo Ala Phe 50 55 60 Agon Ile Val Aso Met Leu His Gly Val Arg Asp Gly Leu Val Arg 70 75 80																
Asp	SO 55 60  Agn Ile Val Agn Met Leu His Gly Val Arg Asp Gly Leu Val Arg																
Ser	Ser																
(2)	INF	ORMA!	rion	FOR	SEQ	ID I	<b>30:</b>	144:									
	44		QUES (A) : (B) : (C) :	leng: Type Strai	edeoi Enu	940 ) :lei: %888	base c ac: : si	pai: id ogle	rs								
	(£x)	) FR	ator:	<b>8</b> :													
			(A) ( (B) ( (D) (	ACOJ.	TION	86	🕸	68	ueno	e:							
	ix)	) Se	ÇUEN	CED:	escr	IPTI:	ON:	SEQ	ID N	D: 1	\$ <b>\$</b> :						
acc	CCAG	rcc '	TÇGA	raga	ar a	atcc	CCTD	C AC	agge	egaç	age	CGAC	cec :	NGGC	CACGTG	•	Q
TCC	GCCA	ccr :	aacu	enaa	ga d	BATC		320		aga Arg					CAA Gln	13	. 2

GGC ACG CCG AAC TOG OTC GAC CTT CAG ACC ACC GAT CAG TCC GCC GCC 160

Gly 30	Thr	Pro	Asn	Trp	Val 15	Asp	Leu	Gln	Thr	Thr 20	Asp	Gin	Ser	Ala	Ala 25	
														ARÇ Asn 40		208
														GGC Gly		286
														GGG Gly		384
														GCG Ala		352
														GCC Als		400
														ACC Thr 130		448
														ACG Thr		496
														GAC Asp		544
														ACC Thr		583
														AAG Lys		\$ <b>4</b> 0
11.0		1.1												GGC Gly 200		688
														gcc Ala		736
														CCG Pro		784
														CAG Gln		832

220

GCG ATC TTC AGT GTG TTG AAG CCC GCA CCG CAG CAA TAGGGAGCAT CCCGGG 884 Ala Ile Phe Ser Val Leu Lys Pro Ala Pro Gln Gln 250 255 360

CASSCCCSCC GGCCGGCASA TTCGGAGAAT GCTAGAAGCT GCCGCCGGCG CCGCCG 940

- (2) INFORMATION FOR SEQ ID NO: 145:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 261 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: protein
  - (v) FRAGMENT TYPE: internal
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 145:

Met Pro Lys Arg Ser Glu Tyr Arg Gln Gly Thr Pro Asn Trp Val Asp 1 5 10

Leu Gln Thr Thr Asp Gln Ser Ala Ala Lys Lys Phe Tyr Thr Ser Leu 20 25 30

She Gly Trp Gly Tyr Asp Asp Asn Pro Val Pro Gly Gly Gly Gly Val 35 40 45

Tyr Ser Met Ala Thr Leu Asn Gly Glu Ala Val Ala Ala Ile Ala Pro SO SS 60

Met Pro Pro Gly Ala Pro Glu Gly Met Pro Pro Ile Trp Asn Thr Tyr

Ile Ala Val Asp Asp Val Asp Ala Val Val Asp Lys Val Val Pro Cly
95 96

Gly Gly Gln Val Met Met Pro Ala Phe Asp Tle Gly Asp Ala Gly Arg 100 105

Met Ser Phe Ile Thr Asp Pro Thr Gly Ala Ala Val Gly Leu Trp Gla 115 120

Ala Asn Arg His Ile Gly Ala Thr Leu Val Asn Glu Thr Gly Thr Leu 130 135 140

The Trp Asn Glu Leu Leu Thr Asp Lys Pro Asp Leu Ala Leu Ala Phe 145 150 150 155

Tyr Glu Ala Val Val Gly Leu Thr His Ser Ser Met Glu Ile Ala Ala 165 170 175

Gly Gln Asn Tyr Arg Val Leu Lys Ala Gly Asp Ala Glu Val Gly Gly 180 185 190

Cys Met Glu Pro Pro Met Pro Gly Val Pro Asa His Trp His Val Tyr 195 205

221

									•								
Phe	Als 210	Val	Asp	Asp	Ala	Asp 215	Ala	The	Ala	Ala	Lys 220	ala	Ala	Ala	Ala		
Gly 225	Sly	Gln	Val	IÌ®	Ala 230	Glu	Pro	Ala	Asp	Ile 235	Pro	Ser	Val	Gly	Arg 246		
Phe	Ala	Val	læu	50r 245	Asp	Pro	Gln	Gly	Ala 250	Ile	Phe	Ser	Val	Leu 255	Lys		
Pro	Ala	Pro	Gln 260	Gln													
(2)	INF(	ORMA'	rion	FOR	982	io i	<b>%</b> 0: :	146:									
	(i)		(A) : (B) : (C) :	CYPE: STRAI POPOS	TK: : : no: :Dedi	200 ) Zlei( WESS	oase C &C: : si	pai: id	rs								
	( 4.76;		(A) ) (B) :		rion:	: 47	2.		37.80L	*							
	(xi	} SR	QUEN	CE DI	SSCR:	IPTI(	DBM : :	SEQ :	ID N	): 18	\$6;						
COG	rarc	GCG :	srec	ACCG4	a c	CCAG	aaga:	a aac	iaadi	agat	CGA			ica ( Pro (			55
								GAG Glu									103
								TTT									151
								gaa Glu									199
								CAG Gln 60							CTC Leu	Ţ	248
gag	TTAC	ccc	cgos	agca	GA C	gcaa:	aaag	e ce									280
(2)	INF	opma	TION	FOR	SEQ	ID 1	MO:	147;									
	<b>(1</b>	) SE	Quen (a)	CE C					id ar								

(D) TOPOLOGY: linear

			kenen Lecui					į.								
	(ix)	SRÇ	guess	ia de	tšcri	pric	110 : S	e Çze	D R	); 16	i7:					
Met 1	Pro	Ğln	Gly	Thr 5	Val	Lys	Trp	Phe	nea 01	Ala	Glu	Lys	Gly	Phe 15	Gly	
Phe	ĭls	Ala	Pro 20	Glu	Asp	Gly	Ser	Ala 25	Asp	Val	Phe	Val	His 30	Tyr	Thr	
Gla	Ila	Gln 35	Gly	Thr	Gly	Phe	Arg 40	Thr	Leu	Clu	Glu	Asn 45	Gln	Lys	Val	
Glu	Phe 50	Glu	lie	Gly	His	Sex 55	Pro	Lys	Gly	Pro	Gln 60	Als	Thr	Gly	Val	
Ary 65	Ser	Leni														
(2)	inf	orma:	rios	FOR	SEQ	II KI	<b>1</b> 0: 3	148:								
	(1)		(A) 1 (A) 1 (B) 7 (C) 1 (D) 7	JENG. Cype Strai	CH: S : Muc IDEDI	ido : Cleic NESS:	3080 3 ac: : si:	pai: id	ćs							
	(ix)	) FE3	NTORE	Z.:												
			(A) 1 (B) 1 (D) (	LOCA	FION	1.08	§ , , , , 4	191	ienc:	>						
	(xi)	SE(	Manc	CE DI	escr:	eri(	IN: 3	gae	id w	): 14	18:					
ATC	37G7;	cor i	ATOSI	AGAA	oc ci	288CX	rogti	a TC	NGAA	2803	CCM	aagex	eca i	aacc	ITTATA	. 60
ACT	rcer	37C (	CCAAJ	argry	ia c	XACC)	47GG	a cci	aagg"	rrcc	TGA	3/33			a CGG su Arg	136
			ACC													184
			GCG Ala													212
			ATC Tle 40													360
			OCC Ala													308

	CCC Pro 70															41	356
	CAA Gln															si	404
	TCG Sex															4	452
	CCG Pro												TAGK	3CGTY	ace ce		203
GCT	CIM	icc e	KGTCC	XII	ic go	ato	ato	) TGK	ertg(	-						d S	540
(2)	INFO	:AMRC	ROZOM	FOR	szç	ID 1	<b>*</b> O: 3	149:									
	(ii)	1803	(A) I (B) 7 (C) I (D) 7	CE C? LENGT TYPE: TYPA! TOPO! LE T?	TH: : : &::::::::::::::::::::::::::::::::	ino : ino : %ESS: : li: pro:	min: :cid : si: :ear :ein	o ac: igle	ids								
	( <b>x</b> i)	SEÇ	)Orm	e di	RSCR:	ip <b>r</b> i	DBF : 8	( Ç88	ID M	): 13	19:						
Met 1	Asn	Leu	Arg	Arg 5	His	Gln	Thr	Leu	Thr 10	Leu	Arg	Leu	Leu	Ala 15	Ala		
Ser	Ala	GJA	Ile 20	Leu	Ser	Ala	Ala	Ala 35	Phe	Ala	Ala	Fro	Ala 30	Gln	Als		
Asn	Pro	Val 35	Asp	Asp	Ala	Phe	Ile 40	Ala	Ala	Leu	Asn	Asn 45	Ala	Gly	Val		
Asn	Tyr 50	Gly	Asp	Pro	Val	Asp 55	Ala	Lys	Ala	Leu	6)y 60	aíĐ	ser	Val	Cys		
Pro 65	Ile	Leu	Ala	Glu	Pro 78	Gly	Gly	Ser	Phe	Asn 75	Thr	Ala	Val	Ala	Ser 80		
Vai	Vai	Ala	Arg	Ala 85	Gln	Gly	Met	Ser	Gln 90	Asp	Met	Ala	Gln	Thr 95	Phe		
Thr	Ser	lle	Ala 100	Ile	Ser	Met.	Тух	Cys 105	Pro	Ser	Val	Met	Ala 110	Asp	Val		
Ala	Ser	Gly 115	Asn	Leu	Pro	Ala	Leu 120	Pro	Asp	Mot	Pro	Gly 125	leu	Pro	Gly		
Car																	

									2	24						
(2)	INFO	emat	TON	FOR	SEQ	ID 3	90: I	150:								
	(2)	() (E	i) Li i) T1 !) S1	NOTE:	i: 40 nucl EDNI	)0 ha Leic 188:	(STI) (Se ) acio sino (Sar	mir: i	3.							
	(ix)	F87	aross	<b>š</b> :												
		ξΞ	i) LC	KATI	:MO	25.	ing : 354 CION:	į.	snce							
	(ix)	44		<b>48</b> 08/1			_pept 35°									
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atae	rtti	300 (	iaack	mon	oc as	Ž			beu S					TTG :		\$1
														GCC Gly -S		99
														AST AST		147
														GCC Ala		198
														TTC Phe		243
														CAA Gin 60		291
														GCC Ala		339
			AAC Asn		TAN	3000	ATG (	cada	rece	at o	ccso	GACC	C 66	Cayo	grog	394

400

(2) INFORMATION FOR SEQ ID NO: 151:

cceass

225

(i) SEQUENCE CHARACTERISTICS:

(A) LEMSTM: 110 amino acids (B) TYPS: amino acid	v.
(D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein	
(*i) SEQUENCE DESCRIPTION: SEQ ID NO: 151:	
Met Arg Leu Ser Leu Thr Ala Leu Ser Ala Gly Val Gly Ala -28 -25 -25	
Met Ser Leu Thr Val Gly Ala Gly Val Ala Ser Ala Asp Pro	Val Asp
Ala Val Ile Aso Thr Thr Cys Aso Tyr Gly Glo Val Val Ala 5 10 15	. Ala Leu 20
Asn Ala Thr Asp Pro Gly Ala Ala Ala Gln Phe Asn Ala Ser 25 30	Pro Val 35
Ala Glo Ser Tyr Leu Arg Aso Phe Leu Ala Ala Pro Pro Pro 40 45 50	**
Ala Ala Met Ala Ala Gin Leu Gin Ala Val Pro Gly Ala Ala 55 60 65	. Gln Tyr
The Gly Leu Val Glu Ser Val Ala Gly Ser Cys Asn Asn Tyr 70 80	
(2) INFORMATION FOR SEQ ID NO: 152:	
(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 990 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: CDNA (ix) FRATURE:	
(A) NAME/KEY: Coding Sequence (B) LOCATION: 93890 (D) OTHER INFORMATION:	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 153:	
AATAGTAATA TOSCTSTGCG GTTGCAAAAC STSTGACCGA GOTTCCSCAS CGGGCCGCCT TCGAGGAGGA CGAACCACAG TC ATG ACG AAC ATC GTG Met Thr Asn Ile Val 1	OTC CTG 113 Val Leu
ATC AAG CAG GTC CCA GAT ACC TGG TCG GAG CGC AAG CTG ACC Ile Lys Gln Val Pro Asp Thr Trp Ser Glu Arg Lys Leu Thr 10 15 20	
GAT TTC ACE CTG GAC CGC GAG GCC GCC GAC GCG GTG CTG GAC	: GAG ATC 209

Asp	Phe 25	Thr	rea	Asp	Arg	Glu 30	Ala	Ala	Asp	Ala	Val 35	Leu	Asp	Glu	Ile	
											CGG Arg					257
											acc Thr					305
											atg Met					353
											TCG Ser					403.
											ATC Ile 115					449
											GTG Val					<b>\$</b> 97
											CAG Gln					545
											GGC Gly					593
											CCC Pro					643.
											TCC Ser 195					683
											acc Thr					737
											GCC Ala					785
											GSS Gly					833
											TAC Tyr					881

227

ARA ATC ATC TAAGACATAC GCACCTCCCA AAGACGAGAG CGATATAACC CATGGCTGA Lys Ile Ile 265 ASTACTOSTS CTCSTTSAGC ACCCTGAAGG CGCGTTAAAG AAGGTCASCG C 990 (2) INFORMATION FOR SEQ ID NO: 153: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 266 amino acids (B) TYPE: amino acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (v) FRAGMENT TYPE: internal (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 153: Met Thr Asn Ile Val Val Leu Ile Lys Gln Val Pro Asp Thr Trp Ser Giu Arg Lys Leu Thr Asp Gly Asp Phe Thr Leu Asp Arg Glu Als Als 28 Asp Ala Val Leu Asp Glu Tie Asn Glu Arg Ala Val Glu Glu Ala Leu Gin Ile Arg Giu Lys Giu Ais Ala Asp Gly Ile Glu Gly Ser Val Thr Val Leu Thr Ala Gly Pro Glu Arg Ala Thr Glu Ala Ile Arg Lys Ala 75 Leu Ser Met Gly Ala Asp Lys Ala Val His Leu Lys Asp Asp Gly Met His Gly Ser Asp Val Ile Glm Thr Gly Trp Ala Lea Ala Arg Ala Leu Gly Thr Ile Glu Gly Thr Glu Leu Val Ile Ala Gly Asn Glu Ser Thr 3350 3.20 128 Asp Gly Val Gly Gly Ala Val Pro Ala Ile Ile Ala Glo Tyr Leo Gly Leu Pro Sin Leu Thr His Leu Arg Lys Val Ser Ile Siu Siy Siy Lys 150 155 Ile Thr Gly Glu Arg Glu Thr Asp Glu Gly Val Phe Thr Leu Glu Als 185 170 The Leu Pro Ala Val Ile Ser Val Asn Glu Lys Ile Asn Glu Pro Arg 185 Phe Pro Ser Phe Lys Gly lie Wet Ala Ala Lys Lys Lys Glu Val Thr 195 200 208

Yal Leu Thr Leu Ala Glu Tie Gly Val Glu Ser Asp Glu Val Gly Leu

	210					215					220					
Ala 225	Asn l	Aia	aty	Ser	Thr 230	Val	Lena	Ala	Ser	Thx 235	Pro	Lys	Pro	Ala	Lys 240	
Thr	Ala (	3ly	Glu	lys 245	Val	Thr	Asp	Glu	Gly 250	<b>Gl</b> u	Gly	Gly	Asn	Gln 255	lle	
Val	Gln '	lyr	Leu 260	Val	Ala	Gln	Lys	Ile 265	Ile							
(2)	impon	RMAT	ROZ	FOR	SEQ	ID 1	<b>90</b> : 3	154:								
	(i)	{2 {¥ {C	() LI () T1 () 81	ingti (PS : (Bani	erra 1: 25 nuci Dedni Dev:	5 ba: leic ESS:	se pa acio sing	sirs 1								
	(xi)	880	)UBN(	ie di	sscr:	(PTI	OM: 1	SBQ :	id m	O: 1.5	\$ <b>4</b> .:					
CTGI	::YTAE)/	TA 7	rgaa/	CCTA	og ge	3GCC										25
(2)	INFO:	rikat	CICM	FOR	seç	ID I	90: :	L55:								
	(\$)	() () ()	i) li i) Ti i) Si	engti /PE : [Ram	Harac H: 3: Huc: Ordni Ogy:	5 ba: leic 858:	se pa acia sina	airs d								
	( <b>x</b> i)	SS(	XJ <b>EN</b> (	CB D	BSCR:	epri(	ON: 3	SWQ :	ed N	D: 11	§S:					
CTC:	Catg	GT J	vocc:	ragg.	AC C		CAGO	c ca	3GC							35
(2)	info	RMA)	MOIS	FOR	SEQ	ID I	₩0::	156:								
	(i)	{2 {3 {3	i) la !) Ti ]) si	engt: fps : fran	Hara: H: 2: Buc: Deds: CX3Y:	9 ba: leic ESS:	se p aci: sin	airs d								
	(ix)	SE(	QUES:	CS D	escr:	ipti:	ON:	SBQ :	ID W	O: 13	ទំគី:					
CIG	ngatc	TA ?	rgago	ecro	rc c	PTGA	ccsc									29
(2)	INFO	ena:	rion	FOR	SEQ	II :	MO:	157:								
	(i)	() () ()	%) 1.3 %) Ti () Si	engt Ype : Tran	Mara: H: 3: nuc: Dedn: COY:	0 ba: leic ESS:	se p aci: sin	airs ā								

100	20	500
	-20	100

i	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 157:	
CTCCC	CCGGGC TTARTAGTTG TTGCAGGAGC	30
(2) 3	INFORMATION FOR SEQ ID NO: 158:	
	(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 33 base pairs  (B) TYPE: nucleic soid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
į	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 158:	
GCTTI	NGATOT ATGATTTTOT GGGCAACCAG GTA	33
(2) 1	INFORMATION FOR SEQ ID NO: 159:	
	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 30 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOFOLOGY: linear	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 159:	
GCTIN	CCATGG GCGAGGCACA GGCGTGGGAA	30
(2)	INFORMATION FOR SEQ ID NO: 160:	
	(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 30 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 160:	
CTGA	GATCTA GAATGCCACA GGGAACTVTG	30
(2)	INFORMATION FOR SEQ ID NO: 161:	
	(i) SEQUENCE CHARACTERISTICS:  {A) LENGTH: 30 base pairs  {B) TYPE: nucleic acid  {C} STRANDEDNESS: single  {D} TOPOLOGY: linear	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 161:	
TCTC	COGGG GTARCYCAGA GCGAGCGGRC	30
(2)	INFORMATION FOR SEC ID NO: 162:	

			230

(1) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 27 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 162:	
CTEAGATCTA TEAACCTCAC CETATCC	27
{2} INFORMATION FOR SEQ ID NO: 163:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 27 base pairs  (B) TYPE: mucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 163:	
TOTOCCGGGG CTCACCCACC GGCCACG	27
(2) INFORMATION FOR SEQ ID NO: 164:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 30 base pairs  (E) TYPE: nucleic acid  (C) STRANDEUNESS: single  (D) TOPOLOGY: linear	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 164:	
CYSAGATCTA TGGCAACACG TYTTATGACG	30
(2) INFORMATION FOR SEQ IS NO: 165:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 30 base pairs  (B) TYPE: nucleic scid  (C) STRANDEDRESS: single  (D) TOPOLOGY: linear	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 165:	
CTCCCCGGGT TAGCTGCTGA GGATCTGCTH	30
(2) INFORMATION FOR SEQ ID NO: 166:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 31 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	

231

(x4) SEQUENCE DESCRIPTION: SEQ ID NO: 166: CTGAAGATCT ATGCCCAAGA GAAGCGAATA C 31 (2) IMPORMATION FOR SEQ ID NO: 167: (i) SEQUENCE CHARACTERISTICS: (A) LEWGTH: 31 base pairs (B) TYPE: nucleic acid {C} STRANDEDNESS: single (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 187: CGCCASCTOC TAGCATTUTC COAATCTOCC G 31. (2) INFORMATION FOR SEQ ID NO: 168: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 15 amino acids (B) TYPE: amino acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: None (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 168: Pro Gln Gly Thr Val Lys Trp Phe Asn Ala Glu Lys Gly Phe Gly (2) INFORMATION FOR SEQ ID NO: 169: (i) SEQUENCE CHARACTERISTICS: (A) LENSTH: 15 amino acids (B) TYPE: amino acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: None (ix) FEATURE: (A) NAME/KEY: Other (B) LOCATION: 15 (D) OTHER INFORMATION: Nam is unknown (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 169: Asm Val Thr Val Ser Ile Pro Thr Ile Leu Arg Pro Xaa Xaa Xaa (2) INFORMATION FOR SEQ ID NO: 170: (i) SECURNCE CHARACTERISTICS:

(A) LEMBTH: 15 amino acids

(B) TYPE: amino acid (C) STRANDEDNESS: single

232

- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: None
- (ix) FEATURE:
  - (A) NAME/KEY: Other
  - (B) LOCATION: 1
  - (D) OTHER INFORMATION: The Could also be Ala
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 170:

Thr Arg Phe Met Thr Asp Pro His Ala Met Arg Asp Met Ala Gly
1 5 10 15

- (2) INFORMATION FOR SEQ ID NO: 171:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 15 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: None
  - (xi) SEQUENCE DESCRIPTION: SEQ TO NO: 171:

Pro Lys Arg Ser Glu Tyr Arg Gln Gly The Bro Asn Trp Val Asp 1 5 10 15

- (2) INFORMATION FOR SEQ ID NO:172:
  - (1) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 404 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - $\{xi\}$  SEQUENCE DESCRIPTION: SEQ ID NO:172:

 Met
 Als
 Thr
 Val
 Asn
 Arg
 Ser
 Arg
 His
 His</th

Ser Ser Phe Tyr Ser Asp Trp Tyr Ser Pro Ala Cys Gly Lys Ala Gly
100 105 110

Cys Sin The Tyr Lys Trp Siu Thr Phe Leu Thr Ser Giu Lau Pro Gin 115 120 125

Trp Leu Ser Ala Asn Arg Ala Val Lys Pro Thr Cly Ser Ala Ala Ile

233

	130					3.35					140				
gly	Les	807	<b>1500</b>	Ala	Gly	Ser	Ser	Ala	zez.	lle	Z#813	Alæ	A18	Tyr	82E
145										155					160
pro	Gin	ar	Pins		xyx	Als	Gly	Ser		Sex	ALA	2:6:3	zea		Pro
				165					170					175	
Ser	Gln	Gly		Gly	32.02	Ser	Legg		Gly	Lossia	ala	Met		yab	Ala
20.90	2009	eec.	180	~~				185	aw v	a.	.No.	A	190	<b>**</b>	no 34
Giy	Gly		Lys	BIB	R18	weez.		Traigh	GTL	Pro	ser	205	SANSES.	3,2,23	Asa
N) 2-25	697 va	195	N. 20.20	No succe	(barre	8998ss	200	ex 2 vs	77.77	Physics	V 4200		T.F.o. V	70.3° as	70. esses
3.2.2.5	Glu 210	Sec. 25.	2585 E.S	week.	8.80	215	32.23.8	22.23	228	E. T. 43.	220	9360.64	7.00.2	****	*****
X.eses	Thr	2000	T 3000	Egyppinger	3.7× 5		eres.	FX 3 40	3.899	reake		See	X.an	Ø1 es	Esseri
225	10.000	www.	,44.47°, 44	n wite.	230	2 T. W.	w't w	O. W.L.	******	238	OK OR ECES	- as .as	2 112111	G1 00 G1	240
	Gly	Ala	Asn	11e	Pro	ala	Glu	Phe	Leu	Glu	Asn	Phe	Val	Arg	Ser
	. •			245					250					255	
Ser	Asn	Leu	Lys	Phe	Gln	Asp	ala	Tyr	Asn	Als	Ala	Gly	Gly	Nis	Asn
			260					365					270		
Ala	val		Asm	2,074	PXO	bxo		Gly	Thr	Ris	262	1787	GLu	Tyr	Try
	*	275					280					285			22.26
Giy	Ala	Gln	Len	ASD	Ala		£3.12	Gly	Amp	Tible 1		Ser	ger	Leu	Gly
v	290	_	_	''		295					300	AN E		-01-5	- A-2
	Gly	TNS	.ijeetji.	Mia		T322.	G3.83	(3131	Gin		MEN	8108	ALS	uay	
305	*3 ~	23.	***	60 mar	320	<b>ም</b> ን		68300	% was	315	693mm	Sam	37 A.	85.5 W	320
(37.72	Ala	wra	337.07	325	247.CE	7.7.45	12.7.27	en T.J.	330	N. CY. T.	2332	2008	8.88	335	CASS 8
Ý.,cov.o	Leu	tions.	88T on		Fares	68.3 mg	(Supre	₹.20094		Š zazed.	3	20.7 20	nia		Trees
AND THE THE	.00 00 00	s.acage	340	ww.z	sage to	W.W.A.D.	And See As.	345	. an ar scan	30 31 03	.000000	2.200.00	380	*****	w.w.th.
Glv	Gly	Ser		Ser	Glu	Alm	The		Glv	Val	Gln	Gln		Trp	Asp
		355					360					365	•	•	
Ala	Thr	Ala	Thr	Gžu	Z.189.E2	A8821	Ann	Ala	Lesu	Gla	Asn	Leu	Ala	Arg	Mir
	370					378					380			•	
Tle	Ser	Glu	$\mathbf{s}i\mathbf{A}$	Gly	Gln	Ala	Met	R1s	Ser	Thr	GLu	Gly	Asn	Val	Thr
385					390					395					400
Cly	Bet	Phe	Ala												

## (2) IMPORMATION FOR SEQ ID NO:173:

## (i) SEQUENCE CHAPACTERISTICS:

- (A) LENGTH: 403 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

# (xi) SEQUENCE DESCRIPTION: SEQ ID NO:173:

				85					90					95	
Ile	Ser	Glu	Ala 100	Gly	Gln	Ala	Met	Ala 105	Ser	Thr	Glu	Gly	Asn 110	Val	Thr
gly	Met	Phe 115	äla	Lys	Læu	Phę	Ser 120	Arg	820	gly	Lighta	Pro 128	Val	Glu	Tyr
Leu	Gln 130	Val	PTO	šer	Pro	Ser 135	Met	Gly	Arg	qeA	11e	Lys	Val	Gln	Phe
Gln 145	Ser	Gly	Sly	Asn	Asn 150	Ser	Pro	Ala	Val	Tyr 155	Leu	leta	Asp	Gly	Leu 160
Arg	Ala	Gln	Asp	Asp 165	Tyr	Asn	Gly	Trp	Asp 170	Il*	Asn	Thr	Pro	Ala 175	Phe
Glu	Try	Tyr	Tyr 180	Gln	Ser	Gly	Leu	Ser 185	Ile	Val	Met	Pro	Val 190	Gly	Gly
		195				_	200	īyr				205	-		
_	210			-		215		Thr			220				
225					230			val		235					240
				245				Ser	250					288	·
His	Pro	Gln	Gln 260	Phe	lle	žàr.	Ala	Gly 265	Ser	Len	Ser	Ala	Leu 270	Leu	Asp
		275	•				280	Leu		•		285		,	**
	290					298		Met			300				
305	-				310			Gln		325					320
				325				Сув	330					335	
		-	340					Glu 345					350		-
Ser	Sex	Ass 355	Leu	Lys	Pho	Sla	Asp 360	Ala	Tyr	Asn	Als	Ala 365	sly	Gly	Mis
	370					375		Asn			380				
385	Gly	Ala	Gln	Leu	Aso 390	Ala	Met	Lys	Gly	Asp 395	Leu	Gln	ser	Ser	Leu 400
Gly	Ala	Gly													

#### CLAIMS

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- 1. A substantially pure polypeptide fragment which
- a) comprises an amino acid sequence selected from the sequences shown in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171,
- b) comprises a subsequence of the polypeptide fragment
  defined in a) which has a length of at least 6 amino

  acid residues, said subsequence being immunologically
  equivalent to the polypeptide defined in a) with
  respect to the ability of evoking a protective immune
  response against infections with mycobacteria belonging
  to the tuberculosis complex or with respect to the

  ability of eliciting a diagnostically significant
  immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the tuberculosis complex, or
- C. comprises an amino acid sequence having a sequence identity with the polypeptide defined in a) or the 20 subsequence defined in b) of at least 70% and at the same time being immunologically equivalent to the polypeptide defined in a) with respect to the ability of evoking a protective immune response against infec-25 tions with mycobacteria belonging to the tuberculosis complex or with respect to the ability of eliciting a diagnostically significant immune response indicating previous or ongoing sensitization with antigens derived from mycobacteria belonging to the tuberculosis com-30 plex,

with the proviso that

- i) the polypeptide fragment is in essentially pure form when consisting of the amino acid sequence 1-95 of SEQ ID NO: 2 or when consisting of the amino acid sequence 87-108 of SEQ ID NO: 4 fused to \$\textit{\textit{g}}\$-galactosidase,
- 5 ii) the degree of sequence identity in c) is at least 95% when the polypeptide comprises a homologue of a polypeptide which has the amino acid sequence SEQ ID NO: 12 or a subsequence thereof as defined in b), and
- iii) the polypeptide fragment contains a threonine residue

  10 corresponding to position 213 in SEQ ID NO: 42 when compri
  sing an amino acid sequence of at least 6 amino acids in SEQ

  ID NO: 42.
  - 2. The polypeptide fragment according to claim 1 in easentially pure form.
- 15 3. The polypeptide fragment according to claim 1 or 2, which comprises an epitope for a T-helper cell.
  - 4. The polypeptide fragment according to any of the preceding claims, which has a length of at least 7 amino acid residues, such as at least 8, at least 9, at least 10, at least 12, at least 14, at least 16, at least 18, at least 20, at least 22, at least 24, and at least 30 amino acid residues.

- 5. The polypeptide fragment according to any of the preceding claims, which is free from amino acid residues -30 to -1 in SBQ ID NO: 6 and/or -32 to -1 in SBQ ID NO: 10 and/or -8 to -1 in SBQ ID NO: 12 and/or -32 to -1 in SBQ ID NO: 14 and/or -33 to -1 in SBQ ID NO: 42 and/or -38 to -1 in SBQ ID NO: 52 and/or -33 to -1 in SBQ ID NO: 56 and/or -56 to -1 in SBQ ID NO: 58 and/or -28 to -1 in SBQ ID NO: 151.
- 6. The polypeptide fragment according to any of the preceding 30 claims which is free from any signal sequence.

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7. The polypeptide fragment according to any of the preceding claims which

- 1) induces a release of IFN-γ from primed memory T-lymphocytes withdrawn from a mouse within 2 weeks of primary infection or within 4 days after the mouse has been rechallenge infected with mycobacteria belonging to the tuberculosis complex, the induction performed by the addition of the polypeptide to a suspension comprising about 200.000 spleen cells per ml, the addition of the polypeptide resulting in a concentration of 1-4 μg polypeptide per ml suspension, the release of IFN-γ being assessable by determination of IFN-γ in supernatant harvested 2 days after the addition of the polypeptide to the suspension, and/or
- 2) induces a release of IFN-y of at least 300 pg above 15 background level from about 1000,000 human PBMC (peripheral blood mononuclear cells) per mi isolated from TB patients in the first phase of infection, or from healthy BCG vaccinated donors, or from healthy contacts to TB patients, the induction being performed by the 20 addition of the polypeptide to a suspension comprising the about 1,000,000 PBMC per ml, the addition of the polypeptide resulting in a concentration of 1-4  $\mu g$ polypeptide per ml suspension, the release of IFN-y being assessable by determination of IFN-y in 25 supernatant harvested 2 days after the addition of the polypeptide to the suspension; and/or
- 3) induces an IFN-γ release from bovine PBMC derived from animals previously sensitized with mycobacteria belonging to the tuberculosis complex, said release being at least two times the release observed from bovine PBMC derived from animals not previously sensitized with mycobacteria belonging to the tuberculosis complex.

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- 8. A polypeptide fragment according to any of the preceding claims, wherein the sequence identity in c) is at least 80%, such as at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 96%, at least 95%, at least 96%, at least 97%, at least 99%, and at least 99.5%.
- 9. A fusion polypeptide comprising at least one polypeptide fragment according to any of the preceding claims and at least one fusion partner.
- 10. A fusion polypeptide according to claim 56, wherein the fusion partner is selected from the group consisting of a polypeptide fragment as defined in any of claims 1-8, and an other polypeptide fragment derived from a bacterium belonging to the tuberculosis complex, such as ESAT-6 or at least one T-cell epitope thereof, MPB64 or at least one T-cell epitope thereof, and MPB69 or at least one T-cell epitope thereof, and
  - 11. A fusion polypeptide fragment which comprises
- 1) a first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope

  20 derived from the M. tuberculosis protein ESAT-6, and a second amino acid sequence including at least one T-cell epitope derived from a M. tuberculosis protein different from ESAT-6 and/or including a stretch of amino acids which protects the first amino acid sequence from in vivo degradation or post-translational processing; or
- 2) a first amino acid sequence including at least one stretch of amino acids constituting a T-cell epitope derived from the M. tuberculosis protein MPTS9, and a second amino acid sequence including at least one T-cell epitope derived from a M. tuberculosis protein different from MPTS9 and/or including a stretch of amino acids which protects the first amino acid

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sequence from in vivo degradation or post-translational processing.

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- 12. A fusion polypeptide fragment according to claim 11, wherein the first amino acid sequence is situated C-terminally to the second amino acid sequence.
  - 13. A fusion polypeptide fragment according to claim 11, wherein the first amino acid sequence is situated N-terminally to the second amino acid sequence.
- 14. A fusion polypeptide fragment according to any of claims 10 11-13, wherein the at least one T-cell epitope included in the second amino acid sequence is derived from a M. tuberculosis polypeptide selected from the group consisting of a polypeptide fragment according to any of claims 1-55, DnaK, GroEL, urease, glutamine synthetase, the proline rich com-15 plex, L-alanine dehydrogenase, phosphate binding protein, Ag 85 complex, HBHA (heparin binding hemagglutinin), MPT51, MPT64, superoxide dismutase, 19 kDa lipoprotein, α-crystallin, GroES, MPT59 when the first T-cell epitope is derived from BSAT-6, and BSAT-6 when the first T-cell epitope is
  - 15. A fusion polypeptide fragment according to any of claims 11-14, wherein the first and second T-cell epitopes each have a sequence identity of at least 70% with the natively occurring sequence in the proteins from which they are derived.
- 25 16. A fusion polypeptide according to any of claims 11-15, wherein the first and/or second amino acid sequence have a sequence identity of at least 70% with the protein from which they are derived.
- 17. A fusion polypeptide fragment according to any of claims
  30 11-16, wherein the first amino acid sequence is the amino
  acid sequence of ESAT-6 or of MPT59 and/or the second amino
  acid sequence is the amino acid sequence of a M. tuberculosis

polypeptide selected from the group consisting of a polypeptide fragment according to any of claims 1-8, DnaK, GroEL, urease, glutamine synthetase, the proline rich complex, L-alanine dehydrogenase, phosphate binding protein, Ag 85 complex. HBHA (heparin binding hemagglutinin). MPT51. MPT64, superoxide dismutase, 19 kDa lipoprotein, a-crystallin, GroES, ESAT-6 when the first amino acid sequence is that of MPT59, and MPT59 when the first amino acid sequence is that of BSAT-6.

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- 18. A fusion polypeptide fragment according to any of claims 10 11-17, which comprises ESAT-6 fused to MPT59.
  - 19. A fusion polypeptide fragment according to claim 18, wherein no linkers are introduced between the two amino acid sequences.
- 20. A polypeptide according to any of the preceding claims 15 which is lipidated so as to allow a self-adjuvating effect of the polypeptide.
  - 21. A substantially pure polypeptide according to any of claims 1-20 for use as a pharmaceutical.
- 20 22. The use of a substantially pure polypeptide according to any of claims 1-20 in the preparation of a pharmaceutical composition for the diagnosis of or vaccination against tuberculosis caused by Mycobacterium tuberculosis, Mycobacterium africanum or Mycobacterium bovis.
- 23. A nucleic acid fragment in isolated form which 25
  - 1) comprises a nucleic acid sequence which encodes a polypeptide as defined in any of claims 1-20, or comprises a nucleic acid sequence complementary thereto,
- has a length of at least 10 nucleotides and hybridizes 2) 30 readily under stringent hybridization conditions with a

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nucleic acid fragment which has a nucleotide sequence selected from SEQ ID NO: 1 or a sequence complementary thereto, SEQ ID NO: 3 or a sequence complementary thereto, Š SEQ ID NO: 5 or a sequence complementary thereto, SEQ ID NO: 7 or a sequence complementary thereto. SEQ ID NO: 9 or a sequence complementary thereto, SEQ ID NO: 11 or a sequence complementary thereto, SEQ ID NO: 13 or a sequence complementary thereto, SEQ ID NO: 15 or a sequence complementary thereto, 0.1 SEQ ID NO: 41 or a sequence complementary thereto, SEQ ID NO: 47 or a sequence complementary thereto, SEQ ID NO: 49 or a sequence complementary thereto. SEQ ID NO: 51 or a sequence complementary thereto, SEQ ID NO: 53 or a sequence complementary thereto, 15 SEQ ID NO: 55 or a sequence complementary thereto, SEQ ID NO: 57 or a sequence complementary thereto, SEQ ID NO: 59 or a sequence complementary thereto, SEQ ID NO: 61 or a sequence complementary thereto, 20 SEQ ID NO: 63 or a sequence complementary thereto, SEQ ID NO: 65 or a sequence complementary thereto, SEQ ID NO: 67 or a sequence complementary thereto. SEQ ID NO: 69 or a sequence complementary thereto, SEQ ID NO: 71 or a sequence complementary thereto, 25 SEQ ID NO: 87 or a sequence complementary thereto, SEQ ID NO: 89 or a sequence complementary thereto, SEQ ID NO: 91 or a sequence complementary thereto, SEQ ID NO: 93 or a sequence complementary thereto, SEQ ID NO: 140 or a sequence complementary thereto, 30 SEQ ID NO: 142 or a sequence complementary thereto, SEQ ID NO: 144 or a sequence complementary thereto, SEQ ID NO: 146 or a sequence complementary thereto, SEQ ID NO: 148 or a sequence complementary thereto, SEQ ID NO: 150 or a sequence complementary thereto, and 35 SEQ ID NO: 152 or a sequence complementary thereto,

with the proviso that when the nucleic acid fragment comprises a subsequence of SEQ ID NO: 41, then the nucleic acid

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fragment contains an A corresponding to position 781 in SEQ ID NO: 41 and when the nucleic acid fragment comprises a subsequence of a nucleotide sequence exactly complementary to SEQ ID NO: 41, then the nucleic acid fragment comprises a T corresponding to position 781 in SEQ ID NO: 41.

- 24. A nucleic acid fragment according to claim 23, which is a DNA fragment.
- 25. A vaccine comprising a nucleic acid fragment according to claim 23 or 24, the vaccine effecting in vivo expression of 0 antigen by an animal, including a human being, to whom the vaccine has been administered, the amount of expressed antigen being effective to confer substantially increased resistance to infections with mycobacteria of the tuberculosis complex in an animal, including a human being.
- 15 26. A nucleic acid fragment according to claim 23 or 24 for use as a pharmaceutical.
  - 27. The use of a nucleic acid fragment according to claim 23 or 24 in the preparation of a pharmaceutical composition for the diagnosis of or vaccination against tuberculosis caused by Mycobacterium tuberculosis, Mycobacterium africanum or Mycobacterium bovis.
    - 28. An immunologic composition comprising a polypeptide according to any of claims 1-20.
- 29. An immunologic composition according to claim 28, which 25 further comprises an immunologically and pharmaceutically acceptable carrier, vehicle or adjuvant.
  - 30. An immunologic composition according to claim 29, wherein the carrier is selected from the group consisting of a polymer to which the polypeptide(s) is/are bound by hydrophobic non-covalent interaction, such as a plastic, e.g. polystyrene, a polymer to which the polypeptide(s) is/are covalently

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tide (MDP).

bound, such as a polysaccharide, and a polypeptide, e.g. bovine serum albumin, ovalbumin or keyhole limpet hemocyanin; the vehicle is selected from the group consisting of a diluent and a suspending agent; and the adjuvant is selected from the group consisting of dimethyldioctadecylammonium bromide (DDA), Quil A, poly I:C, Freund's incomplete adjuvant, IFN-7, IL-2, IL-12, monophosphoryl lipid A (MFL), and muramyl dipep-

- 31. An immunologic composition according to any of claims 28 10 to 30, comprising at least two different polypeptide fragments, each different polypeptide fragment being a polypeptide according to any of claims 1-20.
- 32. An immunologic composition according to claim 31, comprising 3-20 different polypeptide fragments, each different polypeptide fragment being according to any of claims 1-20.
  - 33. An immunologic composition according to any of claims 28-32, which is in the form of a vaccine.
  - 34. An immunologic composition according to any of claims 28-32, which is in the form of a skin test reagent.
- 35. A vaccine for immunizing an animal, including a human being, against tuberculosis caused by mycobacteria belonging to the tuberculosis complex, comprising as the effective component a non-pathogenic microorganism, wherein at least one copy of a DNA fragment comprising a DNA sequence encoding a polypeptide according to any of claims 1-20 has been incor
  - a polypeptide according to any of claims 1.20 has been into:

    porated into the genome of the microorganism in a manner

    allowing the microorganism to express and optionally secrete

    the polypeptide.
- 36. A vaccine according to claim 35, wherein the microorga-30 nism is a bacterium.

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37. A vaccine according to claim 36, wherein the bacterium is selected from the group consisting of the genera Mycobacterium, Salmonella, Pseudomonas and Eschericia.

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- 38. A vaccine according to claim 37, wherein the microorga-5 nism is Mycobacterium bovis BCG, such as Mycobacterium bovis BCG strain: Danish 1331.
- 39. A vaccine according to any of claims 35-38, wherein at least 2 copies of a DNA fragment encoding a polypeptide according to any of claims 1-20 are incorporated into the 10 genome of the microorganism.
  - 40. A vaccine according to claim 39, wherein the number of copies is at least 5.
  - 41. A replicable expression vector which comprises a nucleic acid fragment according to claim 23 or 24.
- 15 42. A vector according to claim 41, which is selected from the group consisting of a virus, a bacteriophage, a plasmid, a cosmid, and a microchromosome.
  - 43. A transformed cell harbouring at least one vector according to claim 41 or 42.
- 44. A transformed cell according to claim 43, which is a 20 bacterium belonging to the tuberculosis complex, such as a M. tuberculosis bovis BCG cell.
  - 45. A transformed cell according to claim 43 or 44, which expresses a polypeptide according to any of claims 1-20.
- 2546. A method for producing a polypeptide according to any of claims 1-20, comprising

inserting a nucleic acid fragment according to claim 23 or 24 into a vector which is able to replicate in a host cell,

introducing the resulting recombinant vector into the host cell, culturing the host cell in a culture medium under conditions sufficient to effect expression of the polypeptide, and recovering the polypeptide from the host cell or culture medium; or

isolating the polypeptide from a short-term culture filtrate as defined in claim 1: or

isolating the polypeptide from whole mycobacteria of the tuberculosis complex or from lysates or fractions thereof, e.g. cell wall containing fractions; or

synthesizing the polypeptide by solid or liquid phase peptide synthesis.

- 47. A method for producing an immunologic composition according to any of claims 28-32 comprising
- preparing, synthesizing or isolating a polypeptide according to any of claims 1-20, and

solubilizing or dispersing the polypeptide in a medium for a vaccine, and

optionally adding other M. tuberculosis antigens and/or a carrier, vehicle and/or adjuvant substance,

 $\alpha x$ 

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cultivating a cell according to any of claims 37-45, and

transferring the cells to a medium for a vaccine, and

25 optionally adding a carrier, vehicle and/or adjuvant substance.

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48. A method of diagnosing tuberculosis caused by Mycobacterium rium tuberculosis, Mycobacterium africanum or Mycobacterium bovis in an animal, including a human being, comprising intradermally injecting, in the animal, a polypeptide according to any of claims 1-20 or an immunologic composition according to claim 34, a positive skin response at the location of injection being indicative of the animal having tuberculosis, and a negative skin response at the location of injection being indicative of the animal not having tuberculosis.

49. A method for immunising an animal, including a human being, against tuberculosis caused by mycobacteria belonging to the tuberculosis complex, comprising administering to the animal the polypeptide according to any of claims 1-20, the immunologic composition according to claim 33, or the vaccine according to any of claims 35-40.

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- 50. A method according to claim 49, wherein the polypeptide, immunologic composition, or vaccine is administered by the parenteral (such as intravenous and intraarterially), intraperitoneal, intramuscular, subcutaneous, intradermal, oral, buccal, sublingual, nasal, rectal or transdermal route.
- 51. A method for diagnosing ongoing or previous sensitization in an animal or a human being with bacteria belonging to the tuberculosis complex, the method comprising providing a blood sample from the animal or human being, and contacting the sample from the animal with the polypeptide according to any of claims 1-20, a significant release into the extracellular phase of at least one cytokine by mononuclear cells in the blood sample being indicative of the animal being sensitized.
- 30 52. A composition for diagnosing tuberculosis in an animal, including a human being, comprising a polypeptide according to any of claims 1-20, or a nucleic acid fragment according to claim 23 or 24, optionally in combination with a means for detection.

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53. A monoclonal or polyclonal antibody, which is specifically reacting with a polypeptide according to any of claims 1-20 in an immuno assay, or a specific binding fragment of said antibody.

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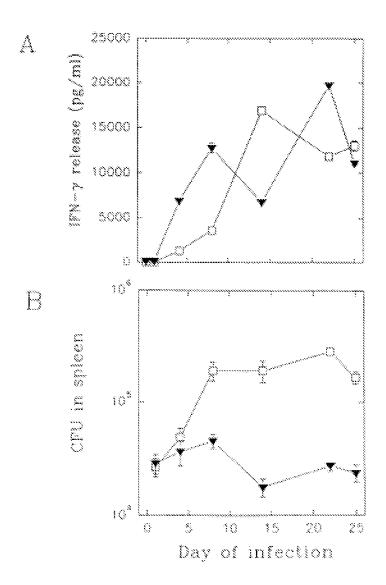


Fig. 1
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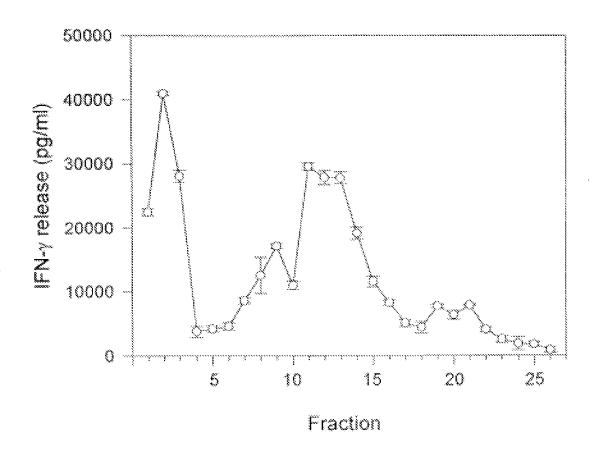


Fig. 2

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51	GGTCGGTCGCCGCTGCTGCGGGCGCTCTGGATTGCCGCACTGTCATTCGG	100
	G R S A L L R A L W I A A L S F G	
101	$\tt GTTGGGGGTGTCGCGGTAGCCGCGGAACCCACCGCCAAGGCCGCCCCAT$	150
	LGGVAVAAEPTAKAAP	
151	ACGAGAACCTGATGGTGCCGTCGCCCTCGATGGGCCGGGACATCCCGGTG	200
	Y E N L M V P S P S M G R D I P V	
201	GCCTTCCTAGCCGGTGGGCCGCACGCGGTGTATCTGCTGGACGCCTTCAA	250
	AFLAGGPHAVYLLDAFN	
251	CGCCGGCCCGGATGTCAGTAACTGGGTCACCGCGGGTAACGCGATGAACA	300
	A G P D V S N W V T A G N A M N	
301	CGTTGGCGGGCAAGGGGATTTCGGTGGTGGCACCGGCCGG	350
	T L A G K G I S V V A P A G G A Y	
351	AGCATGTACACCAACTGGGAGCAGGATGGCAGCAGCAGCAGTGGGACACCTT	400
	SMYTNWEQDGSKQWDTF	
401	CTTGTCCGCTGAGCTGCCCGACTGGCTGGCCGCTAACCGGGGCTTGGCCC	450
	L S A E L P D W L A A N R G L A	
451	CCGGTGGCCATGCGGCCGTTGGCGCCGCTCAGGGGGGGTTACGGGGCGATG	500
	PGGHAAVGAAQGGYGAM	
501	GCGCTGGCGGCCTTCCACCCCGACCGCTTCGGCTTCGCTGGCTCGATGTC	550
	A L A A F H P D R F G F A G S M S	
551	GGGCTTTTGTACCCGTCGAACACCACCACCAACGGTGCGATCGCGGCGG	500
	G F L Y P S N T T T N G A I A A	
601	GCATGCAGCAATTCGGCGGTGTGGACACCAACGGAATGTGGGGGAGCACCA	650
	G M Q Q F G G V D T N G M W G A P	
651	CAGCTGGGTCGGTGGAAGTGGCACGACCCGTGGGTGCATGCCAGCCTGCT	760
	Q L G R W K W H D P W V H A S L L	
701	GGCGCAAAACAACACCCGGGTGTGGGGTGTGGAGCCCGACCAACCCGGGAG	750
	A Q N N T R V W V W S P T N P G	
751	CCAGCGATCCCGCCGCCATGATCGGCCAAACCGCCGAGGCGATGGGTAAC	800
	A S D P A A M I G Q T A E A M G N	
801	AGCCGCATGTTCTACAACCAGTATCGCAGCGTCGGCGGGCACAACGGACA	850
	S R M F Y N Q Y R S V G G H N G H	
851	CTTCGACTTCCCAGCCAGCGGTGACAACGGCTGGGGCTCGTGGGCGCCCC	900
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901	AGCTGGGCGCTATGTCGGGCGATATCGTCGGTGCGATCCGCTAAGCGAAT	950
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Fig. 5

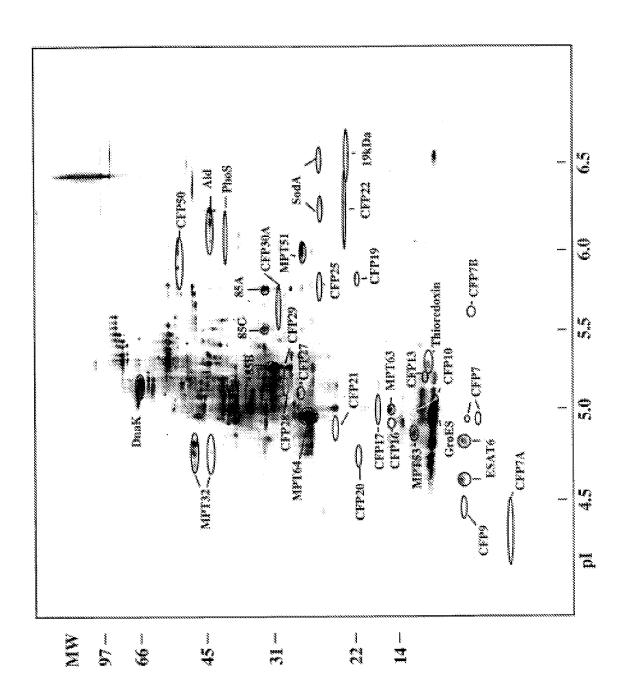


Fig. 6
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% .ssonal Application No. PCT/DK 98/00132

;ANDERSEN PETER (DK); ANDERSEN AASE BENGAAR) 12 January 1995 see the claims see abstract; figure ID; examples 1.3-6; table 2 see page 12 - page 32 see page 12, paragraph 3	1-4,5,7, 9-13,15, 21-43, 45-47, 49-53  1-4,6,7, 20-53  1-4,6,7, 21-24, 28,33, 34, 41-43, 45-53
see the claims see abstract: examples 1.3 see page 12 - page 15. paragraph 2 see page 17. paragraph 4 - page 19. paragraph 2 see page 24 - page 25  WO 95 01441 A (STATENS SERUMSINSTITUT :ANDERSEN PETER (OK): ANDERSEN AASE BENGAAR) 12 January 1995 see the claims see abstract: figure 10: examples 1.3-6: table 2 see page 12 - page 32 see page 12, paragraph 3  SORENSEN A L ET AL: "Purification and characterization of a low-molecular-mass T-cell antigen secreted by Mycobacterium tuberculosis." INFECTION AND IMMUNITY. (1995 MAY) 63 (5) 1710-7. JOURNAL CODE: GO7. ISSN: OD19-9567., XPO02068818 cited in the application see abstract: figures 4-6 see page 1710, paragraph 3 - page 1712, paragraph 4	9-13,15, \$6, 21-43, 45-47, 49-53 1-4,6,7, 20-53 1-4,6,7, 20-53 1-24, 28,33, 34, 41-43,
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Characterization of a low-molecular-mass I-cell antigen secreted by Mycobacterium tuberculosis." INFECTION AND IMMUNITY, (1995 MAY) 63 (S) 1710-7. JOURNAL CODE: GO7. ISSN: OD19-9567., XPOOZO68818 cited in the application see abstract; figures 4-6 see page 1710, paragraph 3 - page 1712, paragraph 4	9.10, 21-24, 28,33, 34, 41-43,
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international application No. PCT/DK 98/06132

### INTERNATIONAL SEARCH REPORT

Boxi	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
Tiris inša	emational Search Report has not been established in respect of cortain claims under Article 17(2)(a) for the following reasons:
1. X	Ciairns Nes.:  Declarise they relate to subject matter not required to be searched by this Authority, namely:
	Although claims 49 and 50 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2 🗍	Claims Nos.: Secure they relate to parts of the international Application that do not comply with the prescribed requirements to such an axion that no meaningful International Search can be carried out, specifically:
	Glasiona Nica::
·	Securities they are dependent idente and are not कंडरेडचे क Sociationse with the second and third sentences of Fule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sines)
This inte	amational Searching Authority found multiple inventions in this international application, as follows:
	see additional sheet
1.	As all required additional search fees were timely paid by the applicant, this international Search Report covers at searchable claims.
2.	As all searchable claims sould be searched without aftert pathying an additional line, this Authority did not invite payment of any additional los.
3. X	As only some of the required additional asarch fees were timely paid by the applicand, this international Search Report covers only those claims for which fees were (wid, specifically claims flos.)
	1-4,6-17,20-53; inventions 1 and 8
4. 🔲	No required solutional search fess were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the diams; it is covered by claims him.
Remark	en Protest  The additional search loss were accompanied by the applicant's protest.
	X 162 protest accompanied the payment of additional search fees
	<del></del>

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-4, 6-17, 20-53 all partially

A polypeptide fragment from mycobacteria belonging to the tuberculosis complex comprising the amino acid SEQ ID NO: 2, nucleic acids endoding said polypeptide as in SEQ ID NO:1, fusion proteins comprising said polypeptides, vaccines, pharmaceutical and immunological compositions containing said polypeptide or nucleic acid, an expression vector comprising said nucleic acid, a host transformed with said vector, immunization with said polypeptide, the use of said polypeptide in diagnosis, antibodies against said polypeptide.

- 2. Claims: 1-4, 6-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 4 and 3.
- 3. Claims: 1-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 6, 5 and 17.
- 4. Claims: 1-4, 6-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 8, 7 and 18.
- 5. Claims: 1-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 10, 9 and 19.
- 6. Claims: 1-17, 20-53 all partially same as invention 1 but for SEO ID NO: 12, 11 and 28.
- 7. Claims: 1-17, 20-53 all partially same as invention 1 but for SEO ID NO: 14, 13 and 21.
- Claims: 1-4, 6-17, 20-53 all partially
   same as invention 1 but for SEQ ID NO: 16, 15 and 23.
- 9. Claims: 1-4, 6-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 22.

- 10. Claims: 1-17, 28-53 all partially same as invention 1 but for SEQ 1D NO: 42 and 41.
- 11. Claims: 1-4, 6-17, 20-53 all partially
  same as invention 1 but for SEQ ID NO: 48, 47 and 81.
- 12. Claims: 1-4, 6-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 50, 49 and 82.
- 13. Claims: 1-17, 20-53 all partially
  same as invention 1 but for SEQ ID NO: 52 and 51.
- 14. Claims: 1-4, 6-17, 20-53 all partially
  5ame as invention 1 but for SEO ID NO: 54, 53 and 83.
- 15. Claims: 1-17, 20-53 all partially
  same as invention 1 but for SEQ ID NO: 56 and 55.
- 16. Claims: 1-17, 20-53 all partially
  same as invention 1 but for SEQ ID NO: 58, 57 and 84.
- 17. Claims: 1-4, 6-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 60, 59 and 85.
- 18. Claims: 1-4, 6-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 62, 61 and 86.
- 19. Claims: 1-4, 6-17, 20-53 all partially
  same as invention 1 but for SEQ ID NO: 64, 63 and 79.
- 20. Claims: 1-4, 6-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 66, 65 and 78.

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 218

- 21. Claims: 1-4, 6-17, 28-53 all partially same as invention 1 but for SEQ ID NO: 68 and 67.
- 22. Claims: 1-4, 6-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 70 and 69.
- 23. Claims: 1-4, 6-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 72 and 71.
- 24. Claims: 1-4, 6-17, 20-53 all partially
  same as invention 1 but for SEQ ID NO: 75.
- 25. Claims: 1-4, 6-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 76.
- 26. Claims: 1-4, 6-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 80.
- 27. Claims: 1-4, 6-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 88 and 87.
- 28. Claims: 1-4, 6-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 90 and 89.
- 29. Claims: 1-4, 6-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 92 and 91.
- 30. Claims: 1-4, 6-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 94 and 93.
- 31. Claims: 1-4, 6-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 141, 140 and 169.

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 218

- 32. Claims: 1-4, 6-17, 20-53 all partially same in invention 1 but for SEQ ID NO: 143, 142 and 170.
- 33. Claims: 1-4. 6-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 145, 144 and 171.
- 34. Claims: 1-4, 6-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 147, 146 and 168.
- 35. Claims: 1-4, 6-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 149, 148 and 73.
- 36. Claims: 1-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 151, 150 and 74.
- 37. Claims: 1-4, 6-17, 20-53 all partially same as invention 1 but for SEQ ID NO: 153, 152 and 77.
- 38. Claims: 11-17, 20-53 all partially, 18, 19

A fusion polypeptide comprising ESAT-6 or MPT59 each individually with one of the following epitope partners: DnaK, GroEL, urease, glutamine synthetase, the proline rich complex, L-alanine dehydrogenase, phosphate binding protein, Ag 85 complex, H8HA, MPT51, MPT64, superoxide dismutase 19 kBa lipoprotein, alpha-crystallin, GroES, nucleic acids endoding said polypeptide, vaccines, pharmaceutical and immunological compositions containing said polypeptide or nucleic acid, an expression vector comprising said nucleic acid, a host transformed with said vector, immunization with said polypeptide, the use of said polypeptide in diagnosis, antibodies against said polypeptide.

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